

tion in dosage of Indocin." "We have had several patients on Indocin develop peptic ulcer disease, and have had two episodes of massive upper GI bleeding." "We feel that there would be certain other studies that should be pursued in the use of Indocin. These would include correlation of blood level with therapeutic effect and with side effects or toxicity. Because of the peculiar mental reactions we have had, we would feel that an attempt to correlate electro-encephalographic findings with blood level and with effect should be done." "We have had considerable disappointment in the amount of side effects" (Oct. 15, 1963).

Dr. JOHN R. WARD,
College of Medicine, University of Utah, Salt Lake City, Utah.

"I would be very anxious to receive further information from you concerning other clinical experiences with Indocin. Our experience to date with the material you supplied us has been limited because of the significant incidence of headaches and gastrointestinal complaints. This has made me reluctant to use it in a number of instances where I might wish to have done so. I would therefore greatly appreciate any further data you have relating to this drug that might influence our use of it" (Jan. 9, 1968).

Dr. KURT J. ISSELBACKER,
*Harvard Medical School,
Massachusetts General Hospital, Boston, Mass.*

"Toxic Manifestations: Only 6 of the 27 failed to show some evidence of toxicity, but in 2 others showing GI toxicity and 1 with rash the medication was continued. Only 1 of the 6 males showing 'excellent' therapeutic response showed clinical toxicity—GI pain" (Jan. 2, 1964).

Dr. WM. C. KUZELL,
San Francisco, Calif.

"I believe you have an excellent skeletal analgesic but I am worried about the headache, nausea and emesis and mental confusion" (Mar. 20, 1963).

Dr. HAROLD M. ROBINS,
Delaware Avenue Medical Center, Buffalo, N.Y.

"In brief, the acute data indicate that indomethacin is approximately as effective as aspirin in the control of fever, joints and other acute manifestations" (Sept. 4, 1963).

Dr. EDWARD A. MORTIMER, JR.,
Cleveland Metropolitan General Hospital, Cleveland, Ohio.

"Dr. Gum continues to find that Indocin is an interesting and effective agent in rheumatoid arthritis. The incidence of headaches, however, is between 85% and 100%. This is causing him real concern. He commented that this would also seriously impair any presentation to FDA. * * * Dr. Burch . . . refuses to do further clinical investigations and is not too happy that any of his staff continues to do them" (May 6, 1963).

Memo R. R. Robert to Dr. N. H. R. Cantwell on "Progress of Study of Indocin" Merck Co.

"The side effects occur in about ten percent of the patients and in nearly one-half of this group, the drug had to be discontinued. The side effects are nausea, headaches and lightheadedness" (Oct. 3, 1963).

Dr. W. D. PAUL,
University Hospitals, University of Iowa, Iowa City, Iowa.

"We also discussed with Dick Rebert we definitely feel that you should set up a double blind on the drug. . . ." "It is with some disappointment that we are reaching the conclusion that the effect of the drug is largely subjective and